Hepatitis B

Hepatitis B remains a major public health problem in the United States, even though a safe and effective vaccine has been available for more than 20 years.

Hepatitis as a distinct clinical entity has been recognized for 2,500 years. It took 2,400 years to recognize that there were more than one type, and that one of these types was transmitted by exposure to human blood or blood products. Only in the last 35 years have we had the laboratory tools to separate hepatitis B from all the other types. Hepatitis B is a disease of enormous global importance as a cause of chronic liver disease and cancer. It is caused by hepatitis B virus, or HBV.

HBV is a small DNA virus, very specific to humans. It is most closely related to viruses which cause hepatitis in woodchucks, ducks, and ground squirrels. The virus has never been grown in tissue culture, which is why the first vaccine was obtained from human carriers. There are several HBV subtypes that do not affect virulence or infectivity, but can be useful in epidemiologic investigations. HBV may retain infectivity outside the body for at least one month at room temperature. Here is a schematic of HBV. The virus has several antigens, but for the purpose of this talk you only need to know about hepatitis B surface antigen. It is shown in this picture as HBsAg. This glycoprotein makes up the outer coat of the virus. Surface antigen itself is not infectious. Only the complete virus, known as the Dane particle, is infectious. But when HBV replicates, it produces surface antigen in huge excess, usually in the form of tubular and spherical structures like you see here. When we find surface antigen in a person's blood, we assume the complete virus is also there, and the person is actively infected, and capable of transmitting the virus. So surface antigen acts as a marker for active infection.

Another thing you need to know about the virus is that antibody to surface antigen indicates immunity to hepatitis B. Other hepatitis B antibodies can be measured, but only the presence of hepatitis B surface antibody indicates protection from infection, either from previous disease or vaccination.

Hepatitis B is a disease of massive proportions. There are an estimated 2 billion new infections worldwide each year. HBV is the most common cause of chronic viremia on the planet. There are estimated to be more than 300 million carriers worldwide. There are estimated to be more than 1 million carriers in the United States. The virus is an established cause of chronic hepatitis and cirrhosis and is estimated to be the cause of up to 80% of hepatocellular carcinomas - liver cancer. Only tobacco is a more frequent cause of cancer than hepatitis B virus. Hepatitis B has a long incubation period, 6 weeks to 6 months, with an average of about 3 months. There may be a nonspecific prodrome of fever, malaise, and headache. The clinical illness is not specific for hepatitis B, and usually includes

anorexia, fatigue, abdominal pain, and jaundice. But at least 50% of infections are asymptomatic. Age is the most important factor in whether an infected person has symptoms. Infection in infants is rarely symptomatic. 10% of older children and 30% of adults will become jaundiced, with a larger percentage having other symptoms of hepatitis.

The most important complication of acute hepatitis B virus infection is fulminant hepatitis, a severe form of acute hepatitis that may lead to acute liver failure. Fulminant hepatitis is estimated to occur in up to 1% of adults with acute hepatitis B virus infection. 10% to 15% of symptomatic infections require hospitalization. The major impact of hepatitis B is not the acute infection. It is the result of chronic carriage of the virus. The most common long term sequelae are cirrhosis and hepatocellular carcinoma. We will come back to chronic carriage in a minute. Death can result from either acute fulminant hepatitis, or from the chronic disease. In the prevaccination era, an estimated 200 to 400 deaths occurred annually from acute fulminant hepatitis. But most of the mortality results from long term carriage of the virus. Every year in the United States an estimated 4,000 to 5,000 persons die from HBV induced liver cancer and cirrhosis. This makes HBV the third most common cause of death among vaccine preventable diseases in the United States, after influenza and pneumococcal disease.

Short of a major breakthrough in the treatment of chronic HBV infection, the number of annual deaths will not change very much anytime soon. That is because it usually takes 20 years or more of chronic infection to result in end stage liver disease. So even if transmission of hepatitis B virus were completely stopped today, deaths from chronic infection would continue to occur for many years to come. This is a Laotian woman with end stage hepatocellular carcinoma from chronic HBV infection. She was probably infected with the virus by her mother when she was born. The enlarged abdomen is a result of a big liver, and ascites, or fluid accumulation in the abdominal cavity. Most persons who die from hepatitis B are chronic carriers. Carriers are persons with chronic viremia. They have virus in their blood and body fluids continuously. Most persons who become carriers will remain carriers the rest of their lives. The overall risk of becoming a carrier is 5% to 10%, and may result from either symptomatic or asymptomatic illness. There are estimated to be about 1.2 million persons chronically infected with HBV in the U.S. now. Several thousand newly infected persons become carriers every year. Although the immunologic mechanism of chronic carriage is not well understood, risk factors for becoming a carrier have been identified. The most important risk factor for chronic carriage of HBV is the **age** of infection. The **earlier** in life infection occurs, the **higher** the risk of becoming a carrier. This graph shows the percent of infected persons who become carriers on the y axis by the age of infection along the x axis. Up to 90% of infants infected at birth will become carriers. Newborn infants are the group most likely to become carriers if they are infected with HBV. 50% of children infected at a year of age will become carriers. By about 5 years of age the risk of becoming a carrier approaches the adult risk of 5 to 10%. Infection early in life is very dangerous because it frequently leads to being a chronic carrier. Chronic carriers are at high risk for morbidity and mortality themselves and remain a source of virus for others for

years. This is why the reduction of perinatal transmission has been one of the priorities of the U.S. hepatitis control program.

Our knowledge of the epidemiology of HBV has driven the vaccination recommendations for the last 20 years. Hepatitis B is a human disease, and the reservoir is humans with acute or chronic infection. It is bloodborne, that is, transmission results from contact with infected blood or body fluids derived from blood. In practice, the only body fluids likely to transmit HBV are blood, vaginal secretions, semen, and maybe saliva on very rare occasions. Persons with asymptomatic infections transmit the virus just the same as symptomatic persons. The virus is communicable 1 to 2 months before and after onset. This graphic shows the number of reported cases of hepatitis B by year since 1978. The first hepatitis B vaccine was licensed in 1981. You might expect a decline in incidence after the vaccine was licensed. But the number of reported cases continued to rise. It peaked in 1985, then slowly declined. It is believed that the decline was not due to vaccine, but to HIV-AIDS education that led to behavioral changes among homosexual men and later among IV drug users. Some of the decline seen since the mid 90s may have been due to vaccine use. In the last 5 years, an average of 9,000 cases of hepatitis B infection have been reported each year. But these **reported** cases only represent a fraction of the actual incidence. It is estimated that in the prevaccine era, 200,000 to 300,000 persons were infected annually with hepatitis B virus, including about 20,000 children. Because of vaccination, and risk reduction behaviors in high risk groups, the number of persons infected in the United States declined to an estimated 79,000 in 2001.

The availability of hepatitis B vaccine had little impact on hepatitis B incidence for the first 10 to 15 years after it was licensed. The most likely reason for this lack of impact was that the vaccine was not reaching the persons at greatest risk of infection. The first strategy of the hepatitis B control program was to identify and vaccinate high risk groups. Two graphs will help you see who is in the target groups. First, the age distribution. This is the age distribution of HBV infection in 1992, a year after the vaccine was added to the routine childhood schedule. Then, as now, the majority of persons who acquired HBV infection are adults. The highest rates were among young adults 20 to 39 years of age. Adolescents accounted for 8% of cases. Childhood and perinatal infection each accounted for about 4%. Four percent may not seem like much. But at that time 200,000 or more persons were newly infected every year. Four percent of 200,000 was 8,000 perinatal and childhood infections each year. Many of these infections are now being prevented with vaccine. During 1986 to 2000, the rate of acute hepatitis B among children aged 1 to 9 years declined by more than 80%. In the last 10 years rates of HBV infection have fallen in all age groups, but continue to be highest in persons 20 to 39 years of age.

Risk factors for infection with HBV have not changed very much in the last 20 years. In the 1980s, sexual contact accounted for more than half of cases, and injection drug users accounted for about 15%. This graphic shows the distribution of risk factors in 2001. Persons with multiple sexual partners, men who have sex

with men, and sexual contact with a person known to have HBV infection account for 54% of cases with a known risk factor. Injection drug use accounts for 20% of cases. About 3% of cases are in persons who have household contact with a person with acute or chronic hepatitis B. Fifteen years ago, healthcare workers accounted for 2% of HBV infections – 2,000 or 3,000 new infections each year. Since that time, the rate of infection among healthcare workers has declined by 95%, and is now lower than the rate for the general population. Hepatitis B vaccine has made occupational HBV infection a thing of the past. So the message from all this is that hepatitis B vaccine has led to a big decline in groups with high vaccination levels – children and health care workers. But thousands of cases are still occurring, mainly among young adults. Reducing the disease burden in this group requires creative vaccination programs to reach high risk adults, particularly in clinics that treat sexually transmitted diseases and injection drug use.

The first hepatitis B vaccine was licensed in the United States in 1981. The hepatitis B surface antigen for the vaccine was purified from the blood of human carriers. In 1986 the first genetically engineered, or recombinant hepatitis B vaccine was licensed. Plasma derived vaccine was taken off the market in 1992.

The vaccine is composed of recombinant hepatitis B surface antigen. The antigen is produced in genetically engineered yeast cells. The yeast cells contain the part of the hepatitis B gene that codes for surface antigen. It does not contain any other part of the hepatitis B virus. The routine hepatitis B vaccine schedule is 3 doses. Vaccine efficacy after a full series is estimated at 95%, with a range of 80% to 100%. The duration of immunity is long, 15 years or more. Routine booster doses are not recommended. Hepatitis B vaccine can and should be administered simultaneously with all other vaccines, in both children and adults. It should be administered intramuscularly, either in the anterolateral thigh of an infant or the deltoid of an older child or adult. No vaccine, including this one, should be administered in the gluteus.

The hepatitis B vaccines available in the U.S. are produced by two different manufacturers- Merck and GlaxoSmithKline. Both companies produce both a pediatric and adult formulation. Recombivax HB from Merck is available in three formulations: a pediatric formulation that contains 5 micrograms per half mL dose; an adult formulation, with 10 micrograms per mL, and a dialysis formulation, with 40 micrograms per mL. Engerix-B from GlaxoSmithKline is available in two formulations: a pediatric formulation with 10 micrograms per half mL dose, and an adult formulation that contains 20 micrograms per mL. The pediatric formulations of both vaccines are available without thimerosal as a preservative.

There are now three combination vaccines that contain hepatitis B vaccine. COMVAX contains hepatitis B and Hib vaccine. Twinrix contains hepatitis B and hepatitis A vaccine and is licensed only for adults. The newest combination vaccine is Pediarix, which contains five antigens – diphtheria, tetanus, acellular

pertussis, hepatitis B, and inactivated polio. We will come back to combination vaccines later.

All infants and children less than 11 years of age receive a half mL dose of either Recombivax OR Engerix. Although the amount of antigen in the half mL doses differs by manufacturer, the vaccines are considered equivalent and are completely interchangeable. Adolescents 11 to 19 years of age should also receive a half mL dose of either Recombivax or the pediatric formulation of Engerix. Adults 20 years and older should receive one mL of either Recombivax or the adult formulation of Engerix. As with the pediatric formulations, the adult formulation of Engerix has twice as much antigen per dose as Recombivax. But the vaccines are considered to be equivalent and are interchangeable. An adult who received one or two doses of adult Recombivax can complete their series with a dose of Engerix, or vice versa. One word of caution – do not be mislead by the higher antigen content of Engerix. The fact that it has twice the antigen per dose does not mean that it is a better vaccine, or that you can give a half dose if you should substitute Engerix for Recombivax. Children should **always** receive a half mL dose, and adults 20 years and older should **always** receive a one mL dose, regardless of which vaccine you are using.

We get a lot of questions about waning immunity to hepatitis B vaccine, and the need for booster doses. It is true that antibody level may decline after vaccination. In fact, up to 60% of recipients may lose detectable antibody by 9 to 15 years after vaccination. But the level of antibody is only part of the issue. Persons who respond to the vaccine develop immunologic memory following vaccination. This means that B lymphocytes have been produced that are primed to produce more hepatitis B surface antibody the next time hepatitis B surface antigen is encountered. We know that this immunologic memory lasts for many years after successful vaccination. Antibody may drop to a low level but an anamnestic, or memory response occurs upon exposure to HBV, and antibody levels increase very quickly. Since the incubation period of HBV is so long, the immune system can mount a protective response before the virus can do any damage. Asymptomatic HBV infection has been occasionally documented in persons who responded to the vaccine. But chronic infection has rarely been documented among vaccine responders. Since chronic infection leads to severe sequelae, and causes most of the mortality, it is what we most want to prevent. Booster doses of hepatitis B vaccine are **not** routinely recommended for any group, because there is no evidence that they are necessary for continued protection. Routine periodic serologic testing to assess the immune status of vaccinated persons is also not recommended, except for persons on dialysis. The duration of hepatitis B immunity following vaccination will continue to be studied for years to come, particularly among those vaccinated as infants. If breakthrough infections, particularly chronic infections, begin to appear 10, 20, or 30 years from now, booster doses may be needed. But not now.

The hepatitis B vaccination strategy has changed several times since the vaccine was licensed in 1981. When new recommendations were made, they did not

replace the prior recommendations. The recommendations were cumulative. So now, hepatitis B vaccine is recommended for persons of many ages.

Hepatitis B vaccine should be administered to all infants without contraindications, preferably beginning at birth. All adolescents through 18 years of age should receive hepatitis B vaccine if they have not already received it. The adolescent visit at 11 or 12 years is a good chance to be sure adolescents are vaccinated. The vaccine should also be given to selected adults. Attempts should continue to be made to vaccinate intermediate and high risk adults, such as men who have sex with men, heterosexuals with multiple partners, injection drug users, and those with an occupational risk of infection. Many adults with acute hepatitis B have received care previously in correctional facilities or STD treatment clinics, where opportunities to vaccinate were missed. CDC is currently working with state and local public health departments to integrate comprehensive hepatitis prevention measures, including hepatitis B vaccination, into programs providing services to adults at risk of HBV infection.

The vaccination schedules are very similar for all age groups. The childhood hepatitis B vaccination schedule recommended by ACIP and the Academy of Pediatrics begins at birth. The second dose is given at one to 2 months of age and the third dose at 6 to 18 months of age. This schedule MUST be used for infants born to women with hepatitis B virus infection, or women whose hepatitis B status is not known at the time of birth. Since 2002, ACIP has stated a preference for the first dose of the hepatitis B series to be administered at birth, before the child leaves the hospital. This strategy assures that the infant will be protected in the event that a woman infected with hepatitis B virus is not detected.

The birth dose is an extremely important safeguard against perinatal transmission of hepatitis B virus. If you are **certain** that the infant's mother is not infected with HBV – meaning she is negative for hepatitis B surface antigen at the time of birth – then the first dose may be given at 1 to 2 months of age. Note the minimum intervals – 1 month between doses one and two, and 2 months between doses 2 and 3. Do not give the vaccine at intervals shorter than these minimums.

The third dose has 3 interval and age rules that you should follow. The third dose should be given a minimum of 2 months after the **second** dose and at least 4 months after the **first** dose. These two rules apply to anyone of any age receiving the vaccine. For infants, there is one more rule. The infant should be at least 24 weeks of age before receiving the third dose. The reason for these three rules is the desire to maximize the response to the vaccine. There are limited data on schedules other than these. If a dose of hepatitis B vaccine is given at an interval or age less than these minimums, the dose should not be counted. The 4 day grace period can be applied to these intervals if your state accepts it.

What about doses that are separated by **longer** than the recommended interval? As with all vaccines routinely used in the U.S., it is not necessary to restart the series or add additional doses if the interval between doses is prolonged. Just

continue the series where it was interrupted. The reason that it is not necessary to restart the series, or to add doses, is because of immunologic memory, which we discussed earlier.

Premature infants with a very low birth weight present a challenge. Infants who weigh less than 2000 grams respond poorly to hepatitis B vaccine. As a result, the first dose of vaccine should be deferred until the child is 1 month old. At a month of age, these infants respond as well as infants of normal birth weight. But this applies only to **routine** hepatitis B vaccination. Postexposure management must be started immediately if the mother is hepatitis B surface antigen positive, or if the mother's surface antigen status is not known, regardless of the child's weight. Postexposure management includes both vaccine and hepatitis B immune globulin, HBIG. There is one other unique aspect of vaccination of low birth weight infants whose mothers are surface antigen positive or unknown: while you should give a dose of hepatitis B vaccine at birth along with HBIG, the American Academy of Pediatrics recommends that this first dose **not be counted**. The infant should receive 3 additional doses, beginning when the infant reaches 1 month of age.

There are now three combination vaccines that contain hepatitis B – Comvax, Pediarix, and Twinrix. Comvax and Pediarix are approved only for children. Twinrix is approved only for adults. Comvax is a combination hepatitis B and Hib vaccine produced by Merck, and was licensed in 1996. Comvax contains a standard 5 microgram dose of Merck's pediatric hepatitis B vaccine, and a standard dose of Merck's Hib vaccine, PedvaxHib. Comvax does not contain thimerosal as a preservative. As with other combinations, the vaccine can be used when either component is indicated and neither antigen is contraindicated. Hib vaccine should not be given to infants less than six weeks of age. So Comvax cannot be used in infants younger than six weeks of age. Although not approved by FDA for this use, Comvax may be used if the infant's mother is known to be surface antigen positive or not known. ACIP approved this off-label use of Comvax in 1997. These infants must receive a birth dose, and the hepatitis B series can be completed with Comvax beginning at 6 to 8 weeks of age.

In December 2002, the Food and Drug Administration licensed a new combination vaccine- Pediarix, which is manufactured by GlaxoSmithKline. This vaccine contains DTaP, inactivated polio and hepatitis B vaccines. The DTaP component is Infanrix, and the hepatitis B component is Engerix-B, which were previously licensed in the U.S. Pediarix is approved for the first three doses of the DTaP and IPV series, which are usually given at about 2, 4, and 6 months of age. However, Pediarix is approved for use through 6 years of age. The minimum age for the first dose of Pediarix is 6 weeks. So it cannot be used for the birth dose of the hepatitis B series. Pediarix may be used in infants born to women who are hepatitis B surface antigen positive or whose hepatitis B status is not known. Like Comvax, Pediarix is not approved by FDA for this use. But in 2003 ACIP approved the off-label use of Pediarix to complete the hepatitis B series for these infants. But remember that the minimum age for Pediarix is 6

weeks, so it must **not** be used for the birth or one month dose of the hepatitis B series. Another important fact to remember about Pediarix is that the minimum intervals between doses are dictated by the single antigen with the longest minimum intervals. Therefore, Pediarix minimum intervals are determined by the hepatitis B component. As for hepatitis B vaccine, the minimum interval between the first two doses of Pediarix is 4 weeks. The third dose must be administered at least 8 weeks after the second dose, and should follow the first dose by at least 16 weeks. The third dose should not be given before 24 weeks of age to be counted as a valid final dose of hepatitis B vaccine.

The third combination vaccine that contains hepatitis B vaccine is Twinrix. Twinrix is produced by GlaxoSmithKline, and was licensed by FDA in 2001. It contains a standard adult dose of GSK's hepatitis B vaccine, Engerix, and a pediatric dose of their hepatitis A vaccine, Havrix. The vaccine is administered in a 3 dose series at 0, 1, and 6-12 months. Twinrix is approved only for persons 18 years of age and older. A pediatric version of Twinrix is not available in the United States. Schedules using combinations of Twinrix and single antigen hepatitis A vaccine have not been studied. We suggest you complete the schedule with the same vaccine that was used for the first dose or doses. If you have your book, please turn to page 210, where there is a discussion of the Twinrix schedule. Contrary to what is in the book at the top of page 210, the spacing of Twinrix doses is based on schedule of the hepatitis A component, not the hepatitis B component. The first and second doses should be separated by at least 4 weeks. The second and third doses should be separated by at least **five months**, not 8 weeks as it says in the book. Please make a note of this error.

Although infants have been our primary emphasis in the last few years, all children and adolescents through age 18 years should be vaccinated. And adults at increased risk of hepatitis B should also be vaccinated. The routine adolescent and adult schedule is 3 doses. For the usual schedule, the first two doses should be separated by at least 1 month, and the third dose is usually given 5 months after the second. If an accelerated schedule is required, the minimum interval between the second and third doses is 2 months. The first dose should **always** be separated from the third dose by at least 4 months. Adolescents should receive ½ mL of pediatric formulation. Adults 20 years and older should receive 1 mL of adult formulation.

In 1999, Merck received FDA approval for an alternative hepatitis B vaccination schedule for adolescents. This alternative schedule is for two **adult** doses – 10 micrograms – of Recombivax HB separated by 4 to 6 months. Seroconversion rates, postvaccination antibody titers, and adverse reactions were similar using this schedule and the standard schedule of three 5 microgram doses of Recombivax HB. This alternative schedule may only be used for adolescents 11 to 15 years of age, and the schedule only applies to Merck's hepatitis B vaccine. I want to repeat this – if you decide to use this 2-dose schedule for adolescents in your practice, it must not be started before age 11 and should be completed by the sixteenth birthday. If the child has already received one or more 5 microgram pediatric doses, he or she should complete the regular 3-dose series, and **not** be

switched to the 2 dose series. Also – Engerix-B is **not** approved for this schedule. This is one situation when the two vaccines are **not** interchangeable. One final note on the 2 dose adolescent schedule: if you decide to use it, please document clearly on the vaccination record – both yours and the personal record – that you gave an adult dose. If you just record hepatitis B vaccine without noting the dose, someone reviewing the record will assume, appropriately, that it was a standard pediatric dose. Please document the doses you administer clearly, and do not make us guess.

We receive many of questions about serologic testing after vaccination. In most circumstances, it is not necessary. Postvaccination serologic testing is **not** recommended after **routine** vaccination of infants, children, adolescents, or most adults. It **is** recommended for infants born to hepatitis B surface antigen positive women – either acutely or chronically infected -- dialysis patients, and immunodeficient persons. In 1997, certain healthcare workers were added to the list.

In December 1997, ACIP and the Hospital Infection Control Practices Advisory Committee published comprehensive recommendations for the immunization of healthcare workers. You should all have a copy of this document. Among many other things, it contains the most recent recommendations for postvaccination serologic testing of healthcare workers. ACIP recommends that healthcare workers who have contact with patients or blood and are at ongoing risk for injuries with sharp instruments or needles should be tested for antibody after vaccination. Routine testing is **not** recommended for persons at low risk of exposure, such as public safety workers and healthcare workers without direct patient contact. Testing for antibody to hepatitis B surface antigen should be done 1 to 2 months after the third dose of vaccine. What about those thousands of healthcare workers who were vaccinated before the 1997 recommendations were published? ACIP does not recommend catch-up serologic testing programs. These persons can be tested as necessary if they are exposed.

Postvaccination serologic testing will occasionally reveal someone who failed to respond to a series of 3 doses that were administered in the correct dosage and route. Persons who do not respond to the first series of 3 doses should complete a second series of three doses or be evaluated to determine if they are already a carrier. The second series should be given on the usual schedule of 0, 1 and 6 months, but an accelerated schedule of 0, 1 and 4 months can also be used. Revaccinated persons should be retested for an antibody response 1 to 2 months after completing the second series.

If you do enough testing you will eventually encounter someone who fails to respond to 6 doses of hepatitis B vaccine. You definitely need to check a surface antigen on these individuals, if this has not already been done. ACIP does not recommend more than 6 total doses. Those who fail to respond to 6 doses and are not surface antigen positive should be assumed to be susceptible and be given postexposure prophylaxis with hepatitis B immune globulin if a high-risk exposure occurs. A table in the healthcare worker recommendations can help

you determine when HBIG is needed. And of course, the person should be counseled about the importance of standard precautions.

Hepatitis B vaccine is inactivated, and adverse reactions following it are similar to other inactivated vaccines. Adverse reactions following hepatitis B vaccine are mostly local. Pain at the injection site is reported in 13% to 29% of recipients. Mild systemic complaints, such as fatigue or headache are reported in 11% to 17% of adults. Temperature of more than 100^{o} Fahrenheit – which is very low grade fever – occurs in only about 1%. Severe systemic reactions are rare. There have been allegations of an association between hepatitis B vaccine and multiple sclerosis. Two well-designed epidemiologic studies have found **no** association between the receipt of hepatitis B vaccine and the onset of multiple sclerosis, or with a relapse in persons already diagnosed with MS. In addition, a 2002 Institute of Medicine report concluded that the weight of the available scientific evidence does **not** support the suggestion that hepatitis B vaccine causes or worsens MS or other demyelinating diseases. These studies and reports are available on the National Immunization Program website.

The contraindications and precautions for hepatitis B vaccine serve as a brief review for those of other inactivated vaccines. The only contraindication is a severe allergic reaction to a vaccine component or following a prior dose. Moderate or severe acute illness is a precaution. Vaccination should be deferred until the acute illness improves.

We do not usually discuss disease management on this program. But we will mention perinatal postexposure prophylaxis because it is such an important intervention. Recall that transmission of hepatitis B virus in the perinatal period leads to chronic carriage for up to 90% of infected infants. The basic recommendations for perinatal management are summarized on this next graphic. For a newborn whose mother is acutely or chronically infected with HBV, begin treatment within 12 hours of birth. In the first 12 hours, give hepatitis B vaccine and HBIG at different sites, for example, each thigh. For infants weighing at least 2,000 grams at birth, give – or ensure that **someone** gives – the second dose at 1 to 2 months of age, and completes the series by 6 months of age. As we mentioned earlier, an infant who weighs less than 2,000 grams at birth and whose mother is seropositive should get a total of 4 doses to complete the series. Test for a response to the vaccine at 9 to 15 months of age – that is, 3 to 9 months after the third dose. Prevention of perinatal and early childhood infection by providing hepatitis B vaccine to newborns is a cornerstone of our hepatitis B prevention strategy. We hope that all of you attending this program will do what you can to assure these important programs are in place in hospitals in your area.